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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/713,669	11/14/2000	Jennifer L. Hillman	PF-0513-1 DIV	3645

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EXAMINER	
PROUTY, REBECCA E	
ART UNIT	**PAPER NUMBER**
1652	11

DATE MAILED: 03/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/713,669	Hillman et al.
Examiner	**Art Unit**
Rebecca Prouty	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 27, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *20-39* is/are pending in the application.

4a) Of the above, claim(s) *22-28 and 31-39* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *20, 21, 29, and 30* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claims 1-19 have been canceled. Claims 21-39 are at issue and are present for examination.

Applicant's election with traverse of Group I, corresponding to current claims 20, 21, 29, and 30 in Paper No. 8 is acknowledged. The traversal is on the ground(s) that coexamination of Groups II, III and V would not require an undue search burden particularly in view of the allowance of the parent application in which Claims within Group II were allowed. This is not found persuasive because while the searches for the four groups overlap, they are not coextensive. The search for Groups II-V would each require the search of subclasses unnecessary for the search of elected Group I. For example, search of Group II would require search of subclasses 435/320.1, and 435/252.3, search of Group III would require search of subclass 530/387.9 and search of Group V would require search of subclass 435/21. While claims within Group II were previously searched in the parent application, the current claims differ from those previously allowed in scope such that a new search would be required to examine these claims. Therefore a substantial additional burden on the examiner would be required to co-examine Group II with Group I.

Newly submitted claims 31-37 and 39 are directed to six inventions that are independent or distinct from the elected

invention and all originally claimed inventions for the following reasons:

Claim 31 is drawn to methods of treating with a human serine protease homolog composition (424/94.6).

Claims 32, 35 and 39 are drawn to methods of screening for modulators of a human serine protease homolog (435/23).

Claim 33 is drawn to agonists of a human serine protease homolog (classification unknown as no structural definition).

Claim 34 is drawn to methods of treating with an agonist a human serine protease homolog (514/789).

Claim 36 is drawn to antagonists of a human serine protease homolog (classification unknown as no structural definition).

Claim 37 is drawn to methods of treating with an antagonist a human serine protease homolog (514/789).

The agonists of Claims 33, antagonists of Claims 34, as well as the products of previous groups I-III each comprise a chemically unrelated structure capable of separate manufacture, use and effect.

The methods of Claims 31 or 32, 35, and 39 and the protein of elected Group I are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different

product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the protein of Group I can be used to induce the antibodies of Group III. The methods of these claims are unrelated to the products of previous Groups II and III.

The products of Claims 33 or 36 and the methods of Claims 32, 34, 35, 37 or 39 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the agonist and antagonist of Claims 33 or 36 can be used as an affinity ligand for the purification of the protein of elected Group I.

The methods of Claims 31, 32, 34, 35, 37 or 39 and previous Groups IV and V are unrelated as they comprise different steps, utilize different products and produce different results.

Accordingly, claims 22-28, and 38 (corresponding to previously defined Groups II-V) and claims 31-37 and 39 (corresponding to newly presented inventions) are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Applicants further request rejoinder of the method claims of Claims 31, 32, 35 and 39 which recite methods of use of the polypeptides of Group I. However, as the corresponding product claims are not currently allowable, rejoinder is not currently required. The applicability of rejoinder will be evaluated upon allowance of the product claims of the elected group.

The requirement is still deemed proper and is therefore made FINAL.

Claim 20 is objected to because of the following informalities: the word "an" following "naturally occurring" in part b) should be deleted. Appropriate correction is required.

Claims 20, 21, 29 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 (upon which Claims 21, 29 and 30 depend) is indefinite in the recitation of "biologically active" as it is unclear what the scope of activities that is encompassed by this term includes. On page 9 of the specification, applicant's define the term "biologically active" as "having structural, regulatory or biochemical functions of a naturally occurring molecule". As the number of naturally occurring molecules is vast, and the scope of possible structural, regulatory or

biochemical functions is even broader with no clear boundaries of what these terms include, the scope of "biologically active fragments" of SEQ ID NO:1 is vague and indefinite.

Claims 20 and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 20 and 29 part c) are directed to polypeptide fragments corresponding to portions of the sequence of SEQ ID NO:1 having any biological activity (see discussion above under 112, 2nd). Claims 20 and 29 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides derived from SEQ ID NO:1 that have not been disclosed in the specification. No description has been provided of the many polypeptide fragments encompassed by the claim. No information, beyond the characterization of SEQ ID NO:1 has been provided by applicants which would indicate that they had possession of the claimed genus of polypeptides. The specification does not contain any disclosure of the function of all the polypeptide fragments derived from SEQ ID NO:1, including fragments within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides

which can have a wide variety of functions. Therefore many functionally unrelated peptide fragments are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Claims 20 and 29 part b) are directed to a genus comprising all naturally-occurring amino acid sequences having 70% sequence identity to the sequence of SEQ ID NO:1. This genus is at least so broad as to encompass all allelic variants of the polypeptide of SEQ ID NO:1 (and might include all allelic variants of other genes if there are multiple homologous loci). The specification defines an "allelic sequence" (see page 8) as an alternative form of the gene which may result in at least one mutation in the nucleic acid sequence. Alleles may result in altered polypeptides whose structure or function may or may not be altered. The definition does not provide any specific information about the structure of naturally occurring (alleles) variants of SEQ ID NO:1 (i.e. where are the regions within which mutations are likely to occur) nor discloses any function for

naturally occurring variants. There is no description of the mutational sites that exist in nature, and there is no description of how the structure of SEQ ID NO:1 relates to the structure of any naturally occurring alleles. The general knowledge in the art concerning alleles does not provide any indication of how one allele is representative of unknown alleles. The nature of alleles is such that they are variant structures, and in the present state of the art, structure and function of one does not provide guidance to the structure and function of others. Thus, the genus of polypeptides claimed is a large variable genus including many functionally unrelated polypeptides within the scope of these claims. The specification discloses only a single species of the claimed genus (i.e SEQ ID NO:1) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 20 and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polypeptides comprising SEQ ID NO:1, consisting of an immunogenic fragment of SEQ ID NO:1 or consisting of a fragment of SEQ ID NO:1 having endooligopeptidase activity, does not reasonably provide enablement for polypeptides consisting of any biologically active fragment of SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 20 and 29 are so broad as to encompass any biologically active fragment of SEQ ID NO:1. On page 9 of the specification, applicant's define the term "biologically active" as "having structural, regulatory or biochemical functions of a naturally occurring molecule". As the number of naturally occurring molecules is vast, and the scope of possible structural, regulatory or biochemical functions is even broader with no clear boundaries of what these terms include, the scope of "biologically active fragments" of SEQ ID NO:1 would appear to include virtually any possible fragment of SEQ ID NO:1 including single amino acids up to large fragments which retain protease activity. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the

extremely large number of biologically active fragments broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which portions of a protein's amino acid sequence have any desired activity requires a knowledge of and guidance with regard to the ways in which the proteins' structure relates to the desired function. However, in this case the disclosure is limited to the structure and function of SEQ ID NO:1.

While recombinant techniques are known which could be used to make many fragments of the polypeptide of SEQ ID NO:1, it is not routine in the art to screen for multiple unknown activities, as encompassed by the instant claims, and the types of activities which may within any fragment of a protein's sequence are vast and unpredictable.

The specification does not support the broad scope of the claims which encompass all biologically active fragments of SEQ ID NO:1 because the specification does **not** establish regions of the protein structure which may be expected to exhibit any particular biological activity nor provide any guidance for predicting which fragments of SEQ ID NO:1 will have any such activity and the specification provides insufficient guidance as

to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any biologically active fragment of SEQ ID NO:1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Hayashi et al. (1996) as evidenced by Hayashi et al. (2000).

Hayashi et al. (1996) teach the purification of rabbit brain endooligopeptidase A.

Hayashi et al. (2000) isolate a partial cDNA clone for the rabbit brain endooligopeptidase A (EOPA) of Hayashi et al. (1996) and teach the sequence of the peptide portion of rabbit EOPA encoded by this cDNA. This sequence includes a portion (aa 57-512) that is 90% identical to the entire length of SEQ ID NO:1.

As the full length rabbit EOPA of Hayashi et al. (1996) clearly comprises the amino acid sequence disclosed by Hayashi et al. (2000), the protein of Hayashi et al. (1996) comprises an amino acid sequence greater that 70% identical to SEQ ID NO:1 and anticipates the instant claims.

Claims 20 and 29 are rejected under 35 U.S.C. 102(b) as being anticipate by the 1997 Sigma catalog product number G 2637.

Page 1159 of the 1997 Sigma Catalog describes the bioactive peptide Glu-Ala-Glu which peptide is a fragment of SEQ ID NO:1 (amino acids 48-50 of SEQ ID NO:1). This anticipates the instant claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy,

can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rebecca Prouty
Primary Examiner
Art Unit 1652